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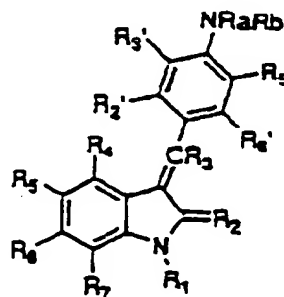
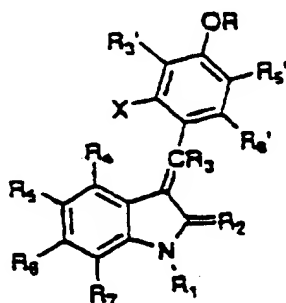
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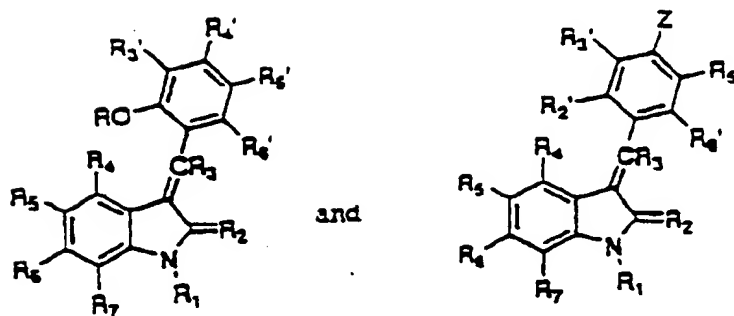
(54) 3-Benzylidene-2-indolinones and their analogues as tyrosine kinase activity modulators

(57) The present invention relates to compounds of the formulae



wherein
X is Br, Cl, F or I;

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wherein

Z is Br, Cl, F, I, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl or tert-butyl;
capable of modulating tyrosine kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation.



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EUROPEAN SEARCH REPORT

Application Number

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	BUZZETTI F ET AL: "Cinnamamide Analogs as Inhibitors of Protein Tyrosine Kinases" IL FARMACO, vol. 48, no. 5, 1993, pages 615-636, XP002103536 * the whole document; in particular, page 631, table II, the compound no.12 *	1,2, 11-18	C07D209/34
X	US 5 206 261 A (KAWAGUCHI AKIHIRO ET AL) 27 April 1993 (1993-04-27) * column 1, line 39 - line 47 * * column 2, line 57 - line 64 *	1,2	
A	WO 91 13055 A (ERBA CARLO SPA) 5 September 1991 (1991-09-05) * page 14, line 7-10 - line 64 * * page 34 - page 35; claim 1 *	1,2, 11-18	
A	EP 0 549 348 A (ERBA CARLO SPA) 30 June 1993 (1993-06-30) * page 12, line 31 - line 36 * * page 14 - page 16, line 36; examples 1,2 * * page 20; claim 1; examples 1,2 *	1,2, 11-18	
E	WO 97 34920 A (SUGEN INC) 25 September 1997 (1997-09-25) * page 39; table II, the compound SU4932 * * page 20; claim 1; examples 1,2 *	1,2	
<p>--- The present search report has been drawn up for all claims</p>			
Place of search		Date of completion of the search	Examiner
MUNICH		25 May 1999	Fink, D
CATEGORY OF CITED DOCUMENTS		<p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document</p>	
<p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p>			

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1, 2, 11-18 (in part)

European Patent
OfficeLACK OF UNITY OF INVENTION
SHEET B

Application Number

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The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1, 2, 11-18 (in part)

the 2-halo-4-(hydroxy/alkoxy/aryloxy)benzylidenyl)-2-indolinone compounds according to the present claims 1 and 2, and the composition/use claims 11-18 (as far as they are directed to the compounds of the present claim 1);

2. Claims: 3-6, 12-18 (in part)

the 3-(4-aminobenzylidenyl)-2-indolinone compounds according to the present claims 3 and 4, the pharmaceutical composition of the present claims 5 and 6, and the use claims 12-18 (as far as they are directed to the compounds of the present claims 3 or 5) ;

3. Claims: 7, 8, 11-18 (in part)

the 3-(2-(hydroxy/alkoxy/aryloxy)benzylidenyl)-2-indolinone compounds according to the present claims 7 and 8, and the composition/use claims 11-18 (as far as they are directed to the compounds of the present claim 7);

4. Claims: 9, 10, 11-18 (in part)

the 3-(4-(halo or C1-C4alkyl)benzylidenyl)-2-indolinone compounds according to the present claims 9 and 10, and the composition/use claims 11-18 (as far as they are directed to the compounds of the present claim 9);

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
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25-05-1999

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82